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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K002023

Submitting Company: MedMira Laboratories
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Date: June 30, 2000

Proprietary Name: MedMira Rapid *H. pylori* Antibody Test

Classification Name: Campylobacter pylori

Device Class: Class I

Product Code: LYR

Predicate Device: *Flexsure HP* test for serum IgG antibodies to *H.pylori*; Manufactured by SmithKline Diagnostics, Inc. (K934863)

Intended Use: The MedMira Rapid *H.pylori* Antibody Test is a rapid, qualitative, visually interpreted immunoassay for the detection of IgG antibodies to *H. pylori* in human serum. The test is to be used in medical diagnostic settings by health care professionals as an aid in the diagnosis of *H. pylori* infection in adult individuals presenting clinical signs and symptoms of gastrointestinal disease.

Device Description: The MedMira Rapid *H. pylori* Antibody Test is a flow-through in vitro diagnostic immunoassay based on the well-established immunological principles of antigen-antibody binding. The test uses a highly purified isolate of *H. pylori* cell lysate as the capture antigen preparation for detecting serum IgG antibodies specific to *H. pylori.* The antigen preparation is immobilized on a nitrocellulose membrane matrix encased within a plastic test tray. When a drop of serum is applied to the membrane surface, the sample flows through the membrane while the specific IgG antibodies to *H. pylori* in the sample bind to the capture antigens on the surface of the membrane. These captured antibodies are visualized when a proprietary protein A-colloidal gold conjugate is added to the surface of the membrane and the conjugate binds to the IgG antibodies. The appearance of a red dot and a red check mark in the center of the test membrane indicates the presence of IgG antibodies to *H. pylori* and can be interpreted as a positive result. If a red check mark appears in the absence of a red dot, this indicates undetectable levels or absence of IgG antibodies specific to *H. pylori* and can be interpreted as a negative result. If neither a red check mark nor a red dot appears, this is indicative of reagent failure and another test should be performed. The red check mark is incorporated into the test as a control to insure the proper functioning of reagents.

Table 1. Similarities and Differences between the MedMira Rapid *H. pylori* Antibody Test and the FlexSure HP predicate device.

	MEDMIRA RAPID *H. PYLORI* ANTIBODY TEST	FLEXSURE HP
Intended Use	The MedMira Rapid *H. pylori* Antibody Test is a rapid, qualitative, visually interpreted immunoassay for the detection of IgG antibodies to *H. pylori* in serum. The test is to be used in medical diagnostic settings by health care professionals as an aid in the diagnosis of *H. pylori* infection in adult individuals presenting clinical signs and symptoms of gastrointestinal disease.	The FlexSure HP test for IgG antibodies to *H. pylori* in serum is a rapid, visually read, qualitative immunochromatographic method. The test is for use by health professionals as an aid in the diagnosis of *H. pylori* infection in patients with clinical signs and symptoms of gastrointestinal disease and is not intended for use with asymptomatic patients.
Sample Type	Serum	Serum
Antibodies Detected	IgG antibodies to *H. pylori*	IgG antibodies to *H. pylori*
Capture Antigen	Proprietary highly purified isolate of *H. pylori* cell	High molecular weight cell-associated protein (HM-

	lysate	CAP)
Built in Control	Yes	Yes
Conjugate Type	Protein A-Colloidal Gold	Colored particles bound to Anti-Human IgG
Storage Temperature	2-8°C or 20-30°C	2-8°C or 15-30°C
Storage at Room Temp.	>6 months	30 days
Suitable for Freezing	No	No
Test Results	Qualitative	Qualitative
Test Type	Rapid flow through	Rapid lateral flow

Discussion of Differences: One of the main differences between the MedMira Rapid *H. pylori* Antibody Test and the predicate Flexsure HP test is that the MedMira test is a flow through device while the Flexsure test is a lateral flow device. In a flow through device, liquids flow vertically downward through membrane materials via gravity. In a lateral flow device, liquids flow horizontally along membrane materials via capillary action. This is not a significant difference between these devices because both types of flow are equally effective in delivering the antibodies contained in the sample to the bound antigens on the membrane surface.

Another difference between these two tests is the conjugate type. The MedMira test uses protein A conjugated to colloidal gold particles as the colored marker that binds to the captured *H. pylori* antibodies. The Flexsure test uses anti-human IgG conjugated to colored particles as the colored marker. This is not a significant difference between these devices because both types of conjugates are equally effective at carrying colored particles and binding to *H. pylori* IgG antibodies.

Finally, the MedMira Rapid *H. pylori* test has a room temperature storage of 6 months compared to the 30 day room temperature storage of Flexsure HP tests. Protein A conjugates are more stable at room temperature than anti-human IgG conjugates.

NONCLINICAL PERFORMANCE DATA:

Validation of Reactive Cutoff: The reactive cutoff of the MedMira Rapid *H. pylori* Antibody Test corresponds to an optical density of greater than or equal to 1.0 in the commercially available Wampole ELISA (Wampole Laboratories, Cranbury, NJ) for *H. pylori* IgG antibodies. A range of dilutions of the capture antigen preparation used in the MedMira test was tested against the Wampole ELISA. The final dilution chosen is the one that allows the highest amount of agreement between the ELISA and the MedMira test. For the final chosen antigen dilution, a total of 247 serum samples (81 positive and 166 negative by the Wampole ELISA) were tested with the MedMira Rapid *H. pylori* Antibody Test. Compared to the Wampole test, the MedMira test results in a sensitivity of 100%, a specificity of 93% and an agreement of 96%.

Interference: The MedMira Rapid Test was evaluated for possible interference from visibly hemolyzed, lipemic and icteric samples and with samples containing

seromarkers other than *H. pylori*. No significant interference was demonstrated in the *H. pylori* positive and negative serum samples.

Cross Reactivity: To evaluate cross reactivity with the MedMira Rapid *H. pylori* Antibody Test, sera containing known amounts of antibodies to *H. pylori* were tested according to the method of Perez-Perez[2] with the following bacteria:
Escherichia coli, Campylobacter coli, Campylobacter fetus, Campylobacter jejuni, Pseudomonas aeruginosa & Helicobacer pylori.
All species tested showed no cross reactivity, indicating that the MedMira Rapid *H. pylori* Antibody Test has a high degree of specificity for human serum antibodies to *H. pylori. Helicobacter pylori* was tested as a control and found to be reactive.

Reproducibility: The reproducibility of the MedMira Rapid *H. pylori* Antibody Test was evaluated both within and between sites. The within site reproducibility of the MedMira Rapid *H. pylori* Antibody Test was evaluated in a blind study using a panel of previously frozen serum samples. The panel consisted of 15 different sera (11 negative, 3 borderline positive and one positive).

Two technicians working independently in the same laboratory performed the MedMira Rapid Test using the panel of 15 sera. Each technician tested each serum sample with two separate lots of the test, 3 tests per lot, for 3 consecutive days. The within site reproducibility was determined to be 100%.

The between site reproducibility of the MedMira Rapid Test was evaluated in blind studies at 3 sites. Each site received from MedMira the same serum panel consisting of 3 high positive samples, 3 borderline positives and 3 negative samples. Each serum sample was tested with 3 tests each day for 3 consecutive days. Results were recorded as either positive or negative. The combined between site reproducibility of the test was determined to be 100%.

Additionally, a lot-to-lot reproducibility study was also performed at one of the sites. Using the same panel, each serum sample was tested with 3 different lots, 3 tests per lot, on one day. The lot-to-lot reproducibility was found to be 100%.

These results indicate that the MedMira Rapid *H. pylori* Antibody Test is accurately reproducible.

Conclusion of non-clinical studies: The non-clinical studies demonstrate that the MedMira Rapid *H. pylori* Antibody Test performs reliably under the anticipated conditions of use.

CLINICAL PERFORMANCE DATA

Two clinical trials were performed to obtain data to support the claim of substantial equivalence between the MedMira and Flexsure tests. The first clinical trial was a prospective study in which the patient population consisted of 210 consecutive patients referred to a Canadian gastroenterology clinic for endoscopy procedure due to complaints of epigastric pain. Antral and stomach biopsies were taken for histology, rapid urease test and culture. Blood samples were collected for serological testing. These tests were performed in different sites in a blinded fashion.

The rapid urease test was performed using the Hpfast test (GI Supply, Camp Hill, PA). Cultures were performed using Wilkens-Chalgren sheep blood agar with DENT selective supplement (Oxoid). The HM-CAP EIA (Enteric Products, Inc., Westbury, NY) served as a reference serology test. The MedMira Rapid *H. pylori* Antibody Test and the Flexsure HP Test were compared to each other and the above standards in order to demonstrate substantial equivalence of the MedMira product to the Flexsure product.

Confirmed positive and negative *H. pylori* infection was based on FDA's DAIDP Points to Consider March 1995 Addendum. A positive culture test, 2 out of 3 or 3 out of 3 positive results from the reference biopsy tests constituted a confirmed positive case. A confirmed negative case is defined as 3 out of 3 or 2 out of 3 negative results from reference biopsy, unless the two negatives are histology and urease in which case the culture would be positive, indicating a confirmed positive result.

Of a total of 210 patients evaluated, there were 86 confirmed positive cases and 124 confirmed negative cases.

When compared to the biopsy reference assays, the MedMira Rapid *H. pylori* Antibody Test was found to have a sensitivity of 94.2%, a specificity of 88.7%, and an overall agreement of 91.0%. This is very comparable to the sensitivity of 91.9%, specificity of 82.3% and overall agreement of 86.2% demonstrated by the Flexsure Test (Table 2).

Table 2. Sensitivity and Specificity of MedMira and Flexsure Tests compared to the biopsy reference tests.

Biopsy Reference Test(s)		MedMira Test		Flexsure Test	
Result	# of cases	Positive	Negative	Positive	Negative
Positive	86	81	5	79	7
Negative	124	14	110	22	102
Total	210	95	115	101	109

Diagnostic Index	MedMira Test	Flexsure Test
Sensitivity	(81/86)=94.2% (89.2, 99.2)*	(79/86)=91.9% (86.1, 97.6)*
Specificity	(110/124)=88.7% (83.1, 94.3)*	(102/124)=82.3% (75.5, 88.9)*
Agreement	(191/210)=91.0% (87.1, 94.8)*	(181/210)=86.2% (81.5, 90.9)*

*95% confidence interval

When the patient serum samples were tested with the reference HM-CAP EIA, 4 samples gave indeterminate readings. If these 4 indeterminates are excluded from the calculations, the MedMira Rapid *H. pylori* Antibody Test was found to have a % agreement positive of 82.6%, and a % agreement negative of 100%. This is very comparable to the % agreement positive of 87.8% and % agreement negative of 100% demonstrated by the Flexsure Test (Table 3).

Table 3. % Agreement Positive & % Agreement Negative of the MedMira and Flexsure Tests compared to the reference EIA test.

ELISA Reference Test		MedMira Test		Flexsure Test	
Result	# of cases	Positive	Negative	Positive	Negative
Positive	115	95	20	101	14
Negative	91	0	91	0	91
Indeterminate	4	0	4	1	3
Total	210	95	115	102	108

Diagnostic Index	MedMira Test	Flexsure Test
% Agreement positive	(95/115)=82.6% (75.7, 89.5)*	(101/115)=86.7% (81.9, 93.8
% Agreement negative	(91/91)=100%	(91/91)=100%

*95% confidence interval

Additionally, the MedMira test was also evaluated retrospectively with a further 348 previously frozen serum samples from symptomatic patients and compared to the reference HM-CAP EIA. All samples were initially tested by the HM-CAP EIA as per the standard practice. An aliquot of these samples was then blindly tested using the MedMira rapid test. Samples yielding either discrepant or indeterminate results were retested using the Flexsure rapid test and the Biorad *H.pylori* IgA EIA test. All tests were carried out and results interpreted according to the manufacturers' instructions.

Results: A total of 348 serum samples were tested in the study. Of these, 205 tested positive for *H.pylori* antibody by the HM-CAP EIA. Of the remaining, 134 were negative and 9 yielded indeterminate result. The MedMira test was positive in 192 (93.7% agreement) of the 205 positive cases, and negative in 133 (99.3% agreement) of the 134 negative cases. The 9 indeterminate results were excluded for data analysis. These findings are summarized in Table 4.

Table 4. Relative performance of the MedMira *H.pylori* Antibody test

HM-CAP EIA		MedMira test	
Result	Number of samples	Positive	Negative
Positive	205	192	13
Negative	134	1	133
Indeterminate	9	4	5
Total	348	197	151

% Agreement positive192/205	93.7	(90.32, 96.99)*
% Agreement negative133/134	99.3	(97.80, 100)

* 95% confidence interval

A second study was performed at a Canadian hospital using previously frozen samples from other *H. pylori* related studies. The MedMira and Flexsure tests were performed by two physicians blinded to the results of the previous studies. The investigators undertook paired testing of serum samples in parallel with the results of each immunoassay being determined independently. Results were then compared and recorded. When findings were discordant, testing was repeated for confirmation.

In this study, 51 previously frozen serum samples from adults involved in a study of intrafamilial clustering of *H. pylori* infection were used.[1] The MedMira test and the Flexsure test were compared to a reference ELISA test.[2] Although the reference ELISA is not considered "Gold Standard" by the FDA guidance document referenced in this 510(k) application, the data are presented here because the author believes it does help to support the claim of substantial equivalence. The MedMira test was found to have a % agreement positive of 86% and a % agreement negative of 90% compared to 82% & 86% respectively for the Flexsure test (Table 5). The results of this study additionally support the claim of substantial equivalence between the MedMira Rapid *H. pylori* Antibody Test and the Flexsure HP Test.

Table 5. % Agreement Positive & % Agreement Negative of MedMira and Flexsure Tests compared to the ELISA reference test.

ELISA Reference Test		MedMira Test		Flexsure Test	
Result	# of cases	Positive	Negative	Positive	Negative
Positive	22	19	3	18	4
Negative	29	3	26	4	25
Total	51	22	29	22	29

Diagnostic Index	MedMira Test	Flexsure Test
% Agreement Positive	19/22=86.36% (72.1, 100)*	18/22=81.82% (65.7, 97.9)*
% Agreement Negative	26/29=89.66% (78.7, 100)*	25/29=86.21% (86.1, 98.6)*

*95% confidence interval

Conclusions from clinical trials: Both the MedMira Rapid *H. pylori* Antibody Test and the Flexsure HP Test have very similar sensitivities, specificities and agreements to both the biopsy and urea breath test "Gold Standard" and EIA reference test. It can therefore be concluded that the results of the clinical trials clearly indicate that the MedMira Rapid *H. pylori* Antibody Test is substantially equivalent to the predicate Flexsure HP Test.

References:

1 Drumm, M.B. et al. 1990. Intrafamilial clustering of *Helicobacter pylori* infection. N. Engl. J. Med. 322 (6):359-363

2. Perez-Perez, G.I. et al. 1988. *Campylobacter pylori* antibodies in humans. Ann. Intern. Med. 109:11-17

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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NOV 13 2000

Mr. Todd D. Bishop
Regulatory Affairs Officer
MedMira Laboratories
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Re: K002023
Trade Name: MedMira Rapid H. pylori Antibody Test
Regulatory Class: I
Product Code: LYR
Dated: October 4, 2000
Received: October 6, 2000

Dear Mr. Bishop:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices); please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(K) Number: K_002023__

Device Name: MedMira Rapid *H. pylori* Antibody Test

Indications For Use:

The MedMira Rapid *H. pylori* Antibody Test is indicated for use in medical diagnostic settings by health care professionals to aid in the diagnosis of *H. pylori* infection in adult individuals presenting clinical signs and symptoms of gastrointestinal disease. The MedMira Rapid *H. pylori* Antibody Test is intended to be a qualitative, visually interpreted immunoassay for the rapid detection of IgG antibodies to *H. pylori* in human serum.

for Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K002023

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use____
(Per 21 CFR 801.109)